REMARKS

Reconsideration and allowance are respectfully requested.

Claims 9, 11 and 20-21 are pending. Amendment of claim 9 is supported by the incorporation of the limitations of claims 10 and 12, as well as the Examiner's statement on pages 3-4 of the Action of the method enabled by the present specification. Dependent claims 10 and 12-15 are canceled because they no longer limit the independent claim after its amendment. New claims 20-21 are based on the working examples of the present specification.

Non-elected claims 1, 5-6 and 16-19 were withdrawn from consideration by the Examiner. Applicant cancels the non-elected claims without prejudice to future prosecution of that subject matter.

It was alleged on page 3 of the Action that a certified copy of the priority document was not filed. But the Examiner cites the requirement for a U.S. application filed under the Paris Convention. Here, this is a U.S. national-stage application filed under the Patent Cooperation Treaty (PCT). In accordance with PCT requirements, Applicant submitted the certified copy to the Receiving Office under PCT Rule 17 (see attached PCT/IB/304 acknowledging receipt thereof) and the International Bureau should have forwarded a copy to each of the designated offices. See also M.P.E.P. § 1893.03(c). Therefore, in accordance with M.P.E.P. § 1896 III, which the Examiner is obligated to obey, he is respectfully requested to consult with the Special Program Examiner in his Technology Center to obtain a certified copy of the priority document. Also see PCT Rule 17.2 which states, "No such Office shall ask the applicant himself to furnish it with a copy." The Examiner is requested to acknowledge that a certified copy of the priority document will be entered into the Image File Wrapper of this application.

35 U.S.C. 112 – Enablement

Claims 9-15 were rejected under Section 112, scope of enablement. Further, the Examiner found that the specification was enabling for "a method of reducing vascular restenosis following thickened endocardial membrane angioplasty in a subject . . ." (see

pages 3-4 of the Action). Applicant traverses because amendment of independent claim 9 in accordance with the Examiner's finding of enablement moots this rejection.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case of obviousness requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. A claim directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 9-13 were rejected under Section 103(a) as allegedly unpatentable over Egashira (J. Gene Med. 7:1588-1589, 2005, which was publicly presented July 2003), Ishikawa et al. (WO 02/14505), and Ishikawa et al. (WO 00/49159). Applicant traverses because the cited documents do not render obvious a hybrid polypeptide comprising

FNCBD and an N-terminal deleted MCP-1, which is encoded by a nucleotide sequence comprising SEQ ID NO: 1. The working examples of Applicant's specification demonstrate that his stent, which provides a gene encoding the hybrid polypeptide, does reduce stenosis. This result is unexpected as admitted by the Examiner in his enablement rejection; there is also no evidence cited in his Action that establishes a reasonable expectation of success to use this stent to reduce vascular restenosis.

The cited documents, alone or in combination, fail to teach or render obvious the claimed gene comprising the nucleotide sequence of SEQ ID NO: 1. The specific site of fusing the FNCBD and N-terminal deleted MCP-1 domains in the hybrid polypeptide is also neither taught nor rendered obvious. Even if it were assumed for the sake of argument that one of ordinary skill in the art would have produced the hybrid polypeptide encoded by SEQ ID NO: 1, no evidence was cited in the Action that the hybrid polypeptide expressed from the eluted gene in host cells would reduce restenosis. Ishikawa (2) is irrelevant to the showing of a reasonable expectation of success since slow release of a polypeptide from a biomaterial cannot be compared to the elution of a gene and its expression in host cells to a sufficient level that restenosis is reduced.

Claims 9-15 were rejected under Section 103(a) as allegedly unpatentable over Palasis et al. (WO 01/74413), Egashira (Hypertension 41:834-841, 2003), Ishikawa et al. (WO 02/14505), and Ishikawa et al. (WO 00/49159). Applicant traverses because the cited documents do not render obvious a hybrid polypeptide comprising FNCBD and an N-terminal deleted MCP-1, which is encoded by a nucleotide sequence comprising SEQ ID NO: 1. The working examples of Applicant's specification demonstrate that his stent, which provides a gene encoding the hybrid polypeptide, does reduce stenosis. This result is unexpected as admitted by the Examiner in his enablement rejection; there is also no evidence cited in his Action that establishes a reasonable expectation of success to use this stent to reduce vascular restenosis.

The cited documents, alone or in combination, fail to teach or render obvious the claimed gene comprising the nucleotide sequence of SEQ ID NO: 1. The specific site of fusing the FNCBD and N-terminal deleted MCP-1 domains in the hybrid polypeptide is also neither taught nor rendered obvious. Even if it were assumed for the sake of argu-

ment that one of ordinary skill in the art would have produced the hybrid polypeptide encoded by SEQ ID NO: 1, no evidence was cited in the Action that the hybrid polypeptide expressed from the eluted gene in host cells would reduce restenosis. Ishikawa (2) is irrelevant to the showing of a reasonable expectation of success since slow release of a polypeptide from a biomaterial cannot be compared to the elution of a gene and its expression in host cells to a sufficient level that restenosis is reduced.

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinarily skill in the art when this invention was made.

Conclusion

Having fully responded to the pending Office Action, Applicant submits that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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